Baclofen Intoxication in a Patient with Chronic Renal Failure

Eurasian Clinical and Analytical Medicine Case Report

Baclofen in Renal Failure

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Abstract
Baclofen is a derivative of γ-aminobutyric acid (GABA), is used in the treatment of spasticity. Baclofen toxicity can cause muscle flaccidity, severe respiratory depression, seizure, coma, bradycardia/tachcardia, or hypotension/hypertension. We report on a 60-year-old female patient with chronic renal failure who presented with stupor due to baclofen intoxication in spite of low dosage.

Keywords
Baclofen Intoxication, Chronic Renal Failure, Impaired Consciousness

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Introduction

Baclofen a β-(p-chlorophenyl) derivative of the neurotransmitter γ-aminobutyric acid (GABA), is currently used in the treatment of muscle spasticity, especially in patients with neurological diseases. Baclofen is eliminated predominantly by the kidneys and patients with impaired renal function have particular risk for baclofen accumulation [1]. Some authors have suggested that haemodialysis is effective in the removal of baclofen, however the pharmakokinetics of baclofen elimination during haemodialysis remains unclear [2]. In this article we report a baclofen intoxication in a patient with chronic renal failure, which was resolved by haemodialysis.

Case Report

A 60-year-old female patient presented at our hospital with nausea, vomiting and impaired consciousness. Her family reported the patient had taken 5 baclofen tablets (50 mg) by mistake six hours previously. Her husband was taking baclofen due to treatment of interactable hiccup. She had hypertension, diabetes mellitus, coroner artery disease, chronic renal failure and congestive heart failure in her past medical history. She was treated by haemodialysis regularly 2 times a week for 18 months. The patient had taken furosemide, amlodipine and carvedilol for antihypertension therapy.

The patient's blood pressure was 150/85 mmHg, heart rate was 108 beats/min and oxygen saturation 96 %. She was afebrile (36,40C) and had vomiting 3 times during emergency monitoring. Laboratory data showed hemoglobine 11,1 g/dl, leukocyte 9700/mm3, with a normal differential count and platelets 236 000/mm3. Serum glucose 299 mg/dl, urea 58 mmol/l and creatinine 2,5 mg/dl, sodium was 137 mmol/l, potassium 5,7 mmol/l, chlorine 112 mmol/L, lactate dehydrogenase 428 U/L (125-220), gamma glutamyl transpeptidase 57 U/L (9-36). The other transaminases were normal. Arterial blood gases showed a limited metabolic acidose and hipoxia, as pH:7,34, pO2:74,3 mmHg, pCO2:36 mmHg, HCO3:19,8 mmol/L, sO2: 95,8 %, Lactat:1,8 mmol/L. Electrocardiography revealed a sinus tachycardia. Chest radiogram had no abnormality.

She had no response to verbal stimulate, eye opening and incomprehensible sounds with pain and withdrawed motor respons to pain. Her pupils were bilateral defected, with neither a direct nor a consensual response to light. She had bilateral babinski sign, but no meningeal irritation signs. Computed tomography (CT) of the brain was normal. While the patient had high blood pressure (220/110 mmHg) and tachcardia (140 beats/min), intensive antihypertension therapy with furosemide and permanent infusion of sodium nitroprusside was started and she was transferred to the intensive care unit. Magnetic resonance imaging (MRI) was performed and showed no abnormality. There was no alteration on her neurological examination and control brain CT was still normal 44 hours after admission. Approximately, her blood pressure was 165/90 mmHg. Electroencephalography was normal.

Over the following 47 hours she had hemodialysis and then was discharged with spontaneous eye opening and incomprehensible sounds. The patient showed dramatic clinical improvement after the second hemodialysis on her 4th day of admission as she was awake and showed cooperation and orientation but retrograde amnesia during the last 2 days. (The patient had acceptance form of medical this article about her disease.)

Discussion

Baclofen is an inhibitory neurotransmitter (GABA receptor agonist) which is a central effected antispasmodic drug. Overdose of baclofen is over 80 mg/day and lethal dosage is 1250-2500 mg/day in adults. The classic clinical presentation of baclofen overdose usually occurs quite rapidly after ingestion. The effects of baclofen intoxication may cover a broad variety of clinical manifestations. These effects include impaired consciousness or coma, generalized muscular hypotonia with absent limb reflexes, respiratory depression, seizures, hemodynamic changes and cardiac abnormalities such as supraventricular tachycardia, bradycardia premature atrial contractions and first-degree heart block, hypotension or hypertension, and either myosis or midriasis [3]. Our patient had impaired consciousness, tachycardia,and mild hypertension 6 hours post ingestion. Chodorowski et. al detected 12/18 patients (66%) admitted to the clinic in deep coma, 10/18 patients (55.5%) with acute respiratory failure and cardiac abnormalities including bradycardia (44.4%), hypertension (33.0%) and hypotension (5.5%) in toxication [1]. Baclofen is rapidly and extensively absorbed and eliminated. Absorption may be dose-dependent, being reduced with increasing doses. Baclofen is excreted primarily by the kidney in unchanged form and there is relatively large intersubject variation in absorption and/or elimination. The patient had toxicity with lower dose despite of classical knowledge. We think that the patient's impaired renal function facilitated this event.

Baclofen toxicity is a clinical diagnosis; measuring plasma level is not possible and results can be misleading. We were unable to measure baclofen level at our institution as the techniques are generally available only in research laboratories. The half-life is 3,5 hours in therapeutic use but a serum half-life of up to 34 hours has been estimated after overdose [5].

The appropriate serum level of baclofen in patients with severely impaired renal function remains unclear. Chen et al. have thought that patients with renal failure are more susceptible to baclofen toxicity [2]. Similarly our patient had toxicity with a low-dose (50 mg). On the other hand as most patients with severely-impaired renal function developed toxic symptoms soon after initiating a low-dose baclofen regimen, the accumulated dosage was small and severe complications were less common. We could not measure the baclofen level, but the patient had severe symptoms.

Chodorowski reported that there was no correlation between the dosage of baclofen and the clinical outcome [4]. This may explain why our patient had severe intoxication symptoms like alteration of consciousness, tachcardia, hypertension, even though she had ingested a low dose of baclofen.

Management of baclofen intoxication is primarily symptomatic. Our patient transferred to the intensive care unit and was treated for hypertension and tachycardia. Gastric lavage and activated charcoal were not used in the patient because they may not be effective if performed over 1 hour after ingestion [6]. The patient was treated with hemodialysis and showed dramatic clinical improvement. Wu et al. measured the changes of baclofen serum concentration during haemodialysis and found that the serum baclofen eliminated up to 79% during the 4 hours of the haemodialysis session [7]. The elimination half-life of baclofen before and during hemodialyses was 15,7 and 3,1 hours.

Conclusion

We report a case presenting with stupor that was associated with acute baclofen intoxication. It's important to be careful in clinical evaluation and to provide full supportive care in baclofen toxicity. Otherwise as demonstrated in our case low dosage can cause baclofen intoxication in patients with impaired renal functions.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement
All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest
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